REMARKS

1. Formal Matters

a. Status of the Claims

Claims 21, 23-25, 27, 28, 35, and 36 are pending in the instant application. Claims 23-25, 27, 28, 35, and 36 are hereby canceled without prejudice to pursuing the canceled subject matter in a continuing application; claim 21 is amended; and claims 41-63 are new. Upon entry of these amendments, claims 21 and 41-63 are pending and under active consideration. Applicant respectfully requests entry of the amendments and remarks made herein into the file history of the instant application.

b. Interview Summary

The undersigned would like to thank Examiners Shin and Zara for the courtesy of the personal interview on May 8, 2007 during which the prior art and amendments to the claims were discussed. This Reply is filed to address the issues raised by the Examiner.

c. Claim Amendments

Previously-presented claim 21 was related to a nucleic acid comprising at least 18 nucleotides of a hairpin precursor (SEQ ID NOs: 128, 131, and 133). Amended claim 21 is related to a nucleic acid comprising at least 18 nucleotides of a miRNA (SEQ ID NO: 477). Specifically, claim 21 is amended to recite that the nucleic acid comprises at least 18 consecutive nucleotides of SEQ ID NO: 477, support for which can be found at Table 1, lines 892-898, and paragraph 1943 of the application as originally filed. Table 1 discloses the hairpin precursor encoded by GAM142 ("P-SEQ ID," or SEQ ID NO: 128), and its corresponding miRNA ("G-SEQID," or SEQ ID NO: 477) as follows:

GENE	PRECURSOR-SEQUENCE	P-SEQID	GENE-SEQ	G-SEQID	FOLD	ED PRECURS	OR			
GAM142	CACCGCCTCTAGATATCGCC	128	CGCCTTTATT	477	C	3	AICG	TITAT	ACATT :	AAATCCA
	TITATTTCCACATTAGATGG		TCCACATTAG		CAC	CCTCTAGAT		TICC	AGATGGT	A
	TAAATCCAATAGTGAAACTA		ATGG		111		I I	1111	1111111	
	TCTTTTTAGGAATGTATGGA				GIG	GGAGATTTG	9 G0	G AAGG	TCTATCA	/
	CTCGCGTTTAGAGGAGTG				A-	-	CGCTCA	TATGT	ATTTT	AAGTGAT

Claim 21, limitation (c) is amended to recite, "a sequence at least 83.3% identical to (a) or (b)," support for which can be found at Table 2, lines 7203-7282 of the application as originally filed. Table 2 discloses that 20 of 24 nucleotides of SEQ ID NO: 477 (encoded by GAM142) (or ~83.3%) are sufficient for binding target mRNAs as shown below for the targeting of the human gene ACADSB:

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New claim 41 recites, "The nucleic acid of claim 21, wherein the nucleic acid comprises SEQ ID NO: 477," support for which can be found as described above for amended claim 21.

New claim 42 recites, "The nucleic acid of claim 21, wherein the nucleic acid comprises SEQ ID NO: 128," support for which can be found as described above for amended claim 21.

New claim 43 recites, "The nucleic acid of claim 21, wherein X=Y," support and antecedent basis for which can be found as described above for claim 21.

New claim 44 recites, "A vector comprising the nucleic acid of any one of claims 21 and 41-43," support for which can be found at paragraph 0023 of the specification as originally filed.

New claim 45 in part recites, "An isolated nucleic acid consisting of X nucleotides," wherein X=21-120, support for which can be found throughout the application as originally filed, including claims 1-3.

New claim 45 also recites that the sequence of the nucleic acid comprises, "(a) Y consecutive nucleotides of SEQ ID NO: 477," wherein Y≥21 and X≥Y, support for which can found as described above for amended claim 21 and at paragraph 0014 of the specification as originally filed.

New claim 45 further recites that the sequence of the nucleic acid comprises, "(b) an RNA equivalent of (a)," support for which can be found as described at paragraph 0014 of the specification as originally filed.

New claim 45 also recites that the sequence of the nucleic acid comprises, "(c) a sequence at least 75.0% identical to (a) or (b)," support for which can be found at Table 2, lines 7203-7282 of the application as originally filed. Table 2 discloses that 18 of 24 nucleotides of SEQ ID NO: 477 (encoded by GAM142) (or ~75.0%) are sufficient for binding target mRNAs as shown below for the targeting human gene LRRFIP1:

New claim 45 further recites that the sequence of the nucleic acid comprises, "(d) the complement of any one of (a)-(c)," support for which can be found at paragraph 0012 of the specification as originally filed.

New claim 46 recites, "The nucleic acid of claim 45, wherein X=Y," antecedent basis and support for which can be found as described above for new claim 45.

New claim 47 recites, "A vector comprising the nucleic acid of claim 45 or 46," support for which can be found at paragraph 0023 of the specification as originally filed.

New claim 48 in part recites, "An isolated nucleic acid consisting of X nucleotides," wherein X=18 to 120, support for which can be found throughout the application as originally filed, including claims 1-3.

New claim 48 also recites that the sequence of the nucleic acid comprises, "(a) Y consecutive nucleotides of SEQ ID NO: 480," wherein Y≥18 and X≥Y, support for which can be found at Table 1, lines 913-919, and paragraphs 0014 and 1985 of the application as originally filed. Table 1 discloses the hairpin precursor encoded by GAM 145 ("P-SEQ ID," or SEQ ID NO: 131), and its corresponding miRNA ("G-SEQID," or SEQ ID NO: 480) as follows:

GENE	PRECURSOR-SEQUENCE	P-SEQID	GENE-SEQ	G-SEQID	FOLDED	PRECURSOR	R			
GAM145	GGCTATTCTGGCGGCTAGAA	131	IGCTATTICG	480	C		IA	TAAT 0	A T	GT
	IGGCATAATCCGGATGTTGT		GCTGCCAGAG		GG TAT	TCTGGCGGC	GAATGGCA	CCG	TGT	G
	GTAGTACAAGTGGCTGCTAT		IGIC		11 111	THITTE	11111111	111	111	
	TICGGCIGCCAGAGIGICC				CC GTG	AGACCGICG	TITATOGT	GGT	ACA	I
					-		7.0	~ /		C.3.

New claim 48 further recites that the sequence of the nucleic acid comprises, "(b) an RNA equivalent of (a)," support for which can be found at paragraph 0014 of the specification as originally filed.

New claim 48 also recites that the sequence of the nucleic acid comprises, "(c) a sequence at least 91.6% identical to (a) or (b)," support for which can be found at Table 2, lines 7383-7412 of the application as originally filed. Table 2 discloses that 22 of 24 nucleotides of SEQ ID NO: 480 (encoded by GAM145) (~91.6%) are sufficient for binding target mRNAs as shown below for the targeting of the human gene LOC197342;

New claim 48 further recites that the sequence of the nucleic acid comprises, "(d) the complement of any one of (a)-(c)," support for which can be found at paragraph 0012 of the specification as originally filed.

New claim 49 recites, "The nucleic acid of claim 48, wherein the nucleic acid comprises SEQ ID NO: 480," support for which can be found as described above for new claim 48.

New claim 50 recites, "The nucleic acid of claim 48, wherein the nucleic acid comprises SEQ ID NO: 131," support for which can be found as described above for new claim 48.

New claim 51 recites, "The nucleic acid of claim 48, wherein X=Y," support for which can be found as described above for new claim 48.

New claim 52, "A vector comprising the nucleic acid of any one of claims 48-51," support for which can be found at paragraph 0023 of the specification as originally filed.

New claim 53 in part recites "An isolated nucleic acid consisting of X nucleotides," wherein X=19 to 120, support for which can be found throughout the application as originally filed, including claims 1-3.

New claim 53 also recites that the sequence of the nucleic acid comprises, "(a) Y consecutive nucleotides of SEQ ID NO; 480," wherein $Y \ge 19$ and $X \ge Y$, support for which can be found as described above for new claim 48.

New claim 53 further recites that the sequence of the nucleic acid comprises, "(b) an RNA equivalent of (a)," support for which can be found at paragraph 0014 of the specification as originally filed.

New claim 53 also recites that the sequence of the nucleic acid comprises, "(c) a sequence at least 83.3% identical to (a) or (b)," support for which can be found at Table 2, lines 7383-7412 of the application as originally filed. Table 2 discloses that 20 of 24 nucleotides of SEQ ID NO: 480 (encoded by GAM145) (or ~83.3%) are sufficient for binding target mRNAs as shown below for the targeting of the human gene KIAA1056:

New claim 53 further recites that the sequence of the nucleic acid comprises, "(d) the complement of any one of (a)-(c)," support for which can be found at paragraph 0012 of the specification as originally filed.

New claim 54 recites, "The nucleic acid of claim 53, wherein X=Y," support for which can be found as described above for new claim 53.

New claim 55 recites, "A vector comprising the nucleic acid of claim 53 or 54," support for which can be found at paragraph 0023 of the specification as originally filed.

New claim 56 recites, "An isolated nucleic acid consisting of X nucleotides," wherein X=20 to 120, support for which can be found throughout the application as originally filed, including claims 1-3.

New claim 56 also recites that the sequence of the nucleic acid comprises, "(a) Y consecutive nucleotides of SEQ ID NO: 482," wherein Y≥20 and X≥Y, support for which can be found at Table 1, lines 927-933, and paragraphs 0014 and 2013 of the application as originally filed. Table 1 discloses the hairpin precursor encoded by GAM147 ("P-SEQ ID," or SEQ ID NO: 133), and its corresponding miRNA ("G-SEQID," or SEQ ID NO: 482) as follows:

GENE	PRECURSOR-SEQUENCE	P-SEQID	GENE-SEQ	G-SEQID	FOLDED	PRECURS	OR			
GAM147	TCTGGTTCTATGTTCCTCGT	133	TCTATGTTCC	482	T	C	- T	rc	: IA	TT
	TTCCTGTATTCTTTTTAAGA		TOGTTTCCTG		TCTGGT	TAT	GTTCCTCG	TC	TG	C
	TCGAGGAACGCCATAATATC		TATT		111111	111	THILLI	11	11	
	AGA				AGACTA	ATA	CAAGGAGC	AG	AT	/
					T	3 000	т.	- 7		TT

New claim 56 further recites that the sequence of the nucleic acid comprises, "(b) an RNA equivalent of (a)," support for which can be found at paragraph 0014 of the specification as originally filed.

New claim 56 also recites that the sequence of the nucleic acid comprises, "(c) a sequence at least 83.3% identical to (a) or (b)," support for which can be found at Table 2, lines 7418-7472 of the application as originally filed. Table 2 discloses 20 of 24 nucleotides of SEQ ID NO: 482 (encoded by GAM147) (~83.3%) are sufficient for binding target mRNAs as shown below for the targeting of the human gene LOC127002, as follows:

New claim 56 further recites that the sequence of the nucleic acid comprises, "(d) the complement of any one of (a)-(c)." support for which can be found at paragraph 0012 of the specification as originally filed.

New claim 57 recites, "The nucleic acid of claim 56," wherein the nucleic acid comprises SEQ ID NO: 482," support for which can be found as described above for claim 56.

New claim 58 recites, "The nucleic acid of claim 56," wherein the nucleic acid comprises SEQ ID NO: 133," support for which can be found as described above for claim 56.

New claim 59 recites, "The nucleic acid of claim 56, wherein X=Y," support for which can be found as described above for new claim 56.

New claim 60 recites, "A vector comprising the nucleic acid of any one of claims 56-59," support for which can be found at paragraph 0023 of the specification as originally filed.

New claim 61 recites, "An isolated nucleic acid consisting of X nucleotides," wherein X=22 to 120, support for which can be found as described throughout the application as originally filed, including claims 1-3.

New claim 61 also recites that the sequence of the nucleic acid comprises, "(a) Y consecutive nucleotides of SEQ ID NO: 482," wherein Y \geq 22 and X \geq Y, support for which can be found as described above for new claim 56.

New claim 61 further recites that the sequence of the nucleic acid comprises, "(b) an RNA equivalent of (a)," support for which can be found at paragraph 0014 of the specification as originally filed.

New claim 61 also recites that the sequence of the nucleic acid comprises, "(c) a sequence at least 75.0% identical to (a) or (b)," support for which can be found at Table 2, lines 7418-7472 of the application as originally filed. Table 2 discloses that 18 of the 24 nucleotides of SEQ ID NO: 482 (encoded by GAM147) (~75.0%) are sufficient for binding target mRNAs for the targeting of the human gene ATP10C, as follows:

New claim 61 further recites that the sequence of the nucleic acid comprises, "(d) the complement of any one of (a)-(c)," support for which can be found at paragraph 0012 of the specification as originally filed.

New claim 62 recites, "The nucleic acid of claim 61, wherein X=Y," support for which can be found as described above for new claim 61.

New claim 63 recites, "A vector comprising the nucleic acid of claim 61 or 62," support for which can be found at paragraph 0023 of the specification as originally filed.

2. Patentability Remarks

a. 35 U.S.C. § 102

(1) 35 U.S.C. § 102(b); Claims 21, 23, and 24

On page 3 of the Office Action, the Examiner rejects claims 21, 23, and 24 under 35 U.S.C. § 102(b) as allegedly being anticipated by Cowsert et al. (US 6,107,091; "Cowsert" hereafter). The Examiner asserts that Cowsert teaches an isolated nucleic acid consisting of 18 nucleotides, the complement of which is at least 67.7% identical to instant SEQ ID NOs; 480 and 131.

Applicant respectfully submits that claims 23 and 24 are canceled without prejudice, thereby rendering the rejection of these claims moot. Amended claim 21 does not recite SEQ ID NO: 480. Nonetheless, new claim 48 is related to a nucleic acid comprising a sequence at least 91.6% identical to 18 or more consecutive nucleotides of SEQ ID NO: 480, and new claim 53 is related to a nucleic acid comprising a sequence at least 83.3% identical to 19 or more consecutive nucleotides of SEQ ID NO: 480. Applicant respectfully submits that, as shown below, Cowsert teaches neither a sequence at least 91.6% identical to 18 or more nucleotides of SEQ ID NO: 480, nor a sequence at least 83.3% identical to 19 or more nucleotides of SEO ID NO: 480.

Accordingly, Cowsert does not teach all the limitations of new claim 48 or 53. In view of the foregoing amendments and remarks, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 21, 23, and 24 under 35 U.S.C. § 102(b).

(2) 35 U.S.C. § 102(b); Claims 21, 23, 24, and 35

On page 3 of the Office Action, the Examiner rejects claims 21, 23, 24, and 35 under 35 U.S.C. § 102(b) as allegedly being anticipated by Robbins *et al.* (WO 2001/30362; "Robbins" hereafter). The Examiner asserts that Robbins teaches isolated nucleic acids consisting of 19 nucleotides (*i.e.*, SEQ ID NOs: 2873, 2874, and 2875) that are at least 67.7% identical to instant SEQ ID NO: 477 and 128.

Applicant respectfully submits amended claim 21 is related to a nucleic acid comprising a sequence at least 83.3% identical to 18 or more consecutive nucleotides of SEQ ID NO: 477, and new claim 45 is related to a nucleic acid comprising a sequence at least 75.0% identical to 21 or more consecutive nucleotides of SEQ ID NO: 477. Applicant respectfully submits that, as shown below, Robbins teaches neither a sequence at least 83.3% identical to 18 or more nucleotides of SEQ ID NO: 477, nor a sequence at least 75.0% identical to 21 or more nucleotides of SEO ID NO: 477.

SEQ ID NO: 477	CGCCTTTATTTCCACATTAGATGG
Robbins 2873	CAACTTAATTTCCACCTTA
Robbins 2874	AACTTAATTTCCACCTTAT
Robbins 2875	ACTTAATTTCCACCTTATT

Accordingly, Robbins does not teach all the limitations of amended claim 21 or new claim 45. In view of the foregoing amendments and remarks, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 21, 23, 24, and 35 under 35 U.S.C. § 102(b).

(3) 35 U.S.C. §§ 102(a) and (e); Claims 21, 23, and 24

On page 4 of the Office Action, the Examiner rejects claims 21, 23, and 24 under 35 U.S.C. §§ 102(a) and (e) as allegedly being anticipated by Bennett et al. (WO 2002/88162; "Bennett" hereafter). The Examiner asserts that Bennett teaches an isolated nucleic acid consisting of 20 nucleotides that is at least 67.7% identical to SEQ ID NOs: 482 and 133

Applicant respectfully submits that amended claim 21 does not recite SEQ ID NOs: 482 or 133. Nonetheless, new claim 56 is related to a nucleic acid comprising a sequence at least 83.3% identical to 20 or more consecutive nucleotides of SEQ ID NO; 482, and new claim 61 is related to a nucleic acid comprising a sequence at least 75.0% identical to 22 or more consecutive nucleotides of SEQ ID NO; 482. Applicant respectfully submits that, as shown below, Bennett teaches neither a sequence at least 83.3% identical to 20 or more nucleotides of SEQ ID NO; 482, nor a sequence at least 75.0% identical to 22 or more nucleotides of SEQ ID NO; 482.

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SEQ ID NO:482 TCTATGTTCCTCGTTTCCTGTATT
Bennett SID#69 GTTCCACTTTTCCTGGATTG
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Accordingly, Bennett does not teach all the limitations of new claim 56 or 61.

On page 4 of the Office Action, the Examiner also asserts that SEQ ID NO: 61 of Bennett is at least 67.7% identical to SEQ ID NO: 128. Applicant respectfully submits that amended claim 21 does not recite SEQ ID NO: 128. Nonetheless, claim 21 is related to a nucleic acid at least 83.3% identical to SEQ ID NO: 477 and new dependent claim 42 is related to a nucleic acid comprising SEQ ID NO: 128. Applicant respectfully submits that, as shown below, Bennett does not teach a sequence at least 83.3% identical to SEQ ID NO: 477 or SEQ ID NO: 128.

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SID#128 CACCGCCCTAGATATCGCCTTTATTCCA-CATTAGA-TGGTAAATCCAATAGTGAAACTATCTTTTTAGGAATGTATGGACTGGGTTTAGAGGAGTG
SID#477 CGCCTTTATTCCA-CATTAGA-TGG
Bennett SID#61 GGGGACAG-A-TGG-AATCCA
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Accordingly, Bennett does not teach all the limitations of amended claim 21 or new claim 42. In view of the foregoing amendments and remarks, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 21, 23, and 24 under 35 U.S.C. §§ 102(a) and (e).

(4) 35 U.S.C. § 102(e); Claims 21 and 24

On page 4 of the Office Action, the Examiner rejects claims 21 and 24 under 35 U.S.C. § 102(e) as allegedly being anticipated by Aldwinckle et al. (US 6.903,247; "Aldwinckle" hereafter). The Examiner asserts that Aldwinckle teaches an isolated nucleic acid, the complement of which is at least 67.7% identical to SEQ ID NO: 131.

Applicant respectfully submits that amended claim 21 does not recite SEQ ID NO: 131. However, the nucleic acids of new claims 48, 50, and 53 are related to SEQ ID NO: 131. Applicant submits that, as shown below, Aldwinckle does not teach a sequence at least 91.6% identical to 18 or more nucleotides of SEQ ID NO: 480, a sequence at least 83.3% identical to 19 or more nucleotides of SEQ ID NO: 480, or the sequence of SEQ ID NO: 131.

```
SEQ ID NO: 131 GGCTATTCTGGCGGCTAGAATGGCATAATCCGGATGTTGTGTAGTACAAGTGGCTGCTATTTCGGCTGCCAGAGTGTCC
SEQ ID NO: 480
Aldwinckle 19 GCACAAGTGCCTGCTATTX 2
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Accordingly, Aldwinckle does not teach all the limitations of new claims 48, 50, or 53. In view of the foregoing amendments and remarks, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 21 and 24 under 35 U.S.C. § 102(e).

b. 35 U.S.C. § 103(a); Claims 21, 23-25, 27, 28, 35, and 36

On pages 5 and 6 of the Office Action, the Examiner rejects claims 21, 23-25, 27, 28, 35, and 36 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Robbins in view of Fire et al. (US 6,506,559; "Fire" hereafter). The Examiner asserts that Robbins teaches isolated nucleic acids consisting of 19 nucleotides that are at least 67.7% identical to instant SEQ ID NO: 477. The Examiner further asserts that the sequences of these nucleic acids are cyclin H ribozyme binding sites. The Examiner also asserts that Fire teaches that nucleic acid

sequences may be optimized by alignment algorithms known in the art, and therefore that the nucleic acid sequences may comprise insertions, deletions, or point mutations, or may be 100% identical to targets of the nucleic acids. The Examiner asserts that it would have been *prima facie* obvious to one of skill to optimize the sequence of Robbins SEQ ID NO: 2873 by using the algorithms taught by Fire, order to increase the efficacy or degree of target gene inhibition.

In view of the foregoing amendment and remarks set forth below, Applicant respectfully disagrees. Applicant submits that the differences between the Robbins sequence and the miRNA sequence encoded by GAM142 (SEQ ID NO: 477) would be expected to lead to differences in binding of target sequences and inhibition. Fire does nothing to overcome the failings of Robbins to identify the same target gene mRNAs as the claimed invention. Accordingly, the nucleic acids of amended claim 21, and new claims 41 and 42 are not obvious as compared to the Robbins sequences in view of Fire. In view of the foregoing amendment and remarks, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 21, 23-25, 27, 28, 35, and 36 under 35 U.S.C. § 103(a).

3. Conclusion

312.602.3955 (E-fax) 312.873.3613 (direct)

Applicant respectfully submits that the instant application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

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